Science Advisory Board (SAB)
Supplemental Guidance for Assessing Cancer Susceptibility (SGACS) Review Panel
Teleconference Meeting
April 24, 2003 – U.S. EPA, Washington, DC

Panel Members: See Panel Roster (Attachment A)

Date and Time: Thursday, April 24, 2003, 3:00 to 5:00 p.m. EDT

Location: U.S. Environmental Protection Agency
Ariel Rios Federal Building, Room 6013
1200 Pennsylvania Avenue NW
Washington, DC 20005

Purpose: The purpose of this public teleconference meeting was to begin the review of the EPA Office of Research and Development (ORD) draft document titled, "Supplemental Guidance for Assessing Cancer Susceptibility From Early-Life Exposure to Carcinogens" (SGACS).

Attendees:

Chair:	Dr. Henry Anderson
SAB Members:	Dr. David Hoel Dr. Richard Hornung Dr. James Klaunig Dr. Ulrike Luderer Dr. Anne Sweeney Dr. Richard Vetter
CHPAC Members:	Dr. Daniel Goldstein Dr. Melanie Marty
SAP Members:	Dr. Stuart Handwerger Dr. Steven Heeringa Dr. Christopher Portier
EPA SAB Staff:	Dr. Suhair Shallal Dr. Vanessa Vu Mr. Robert Flaak

Other Persons Attending:
(in order of their appearance on the Agenda)

Mr. Ken Wernick, Senior Ethics Counsel, U.S. EPA
Dr. Bill Wood, U.S. EPA, Risk Assessment Forum (RAF)

Via telephone:
Dr. Hugh Barton, U.S. EPA
Nancy Beck, OMB
Dr. Deborah Cory-Slechta, University of Rochester, member SAB EHC
Lynn Ehrle, Cancer Prevention Coalition
Lynn Flowers, U.S. EPA
Steve Knott, U.S. EPA
Pat Phibbs, BNA

Other EPA personnel and members of the public, as noted on the sign-in sheet.

Meeting Summary

The meeting generally followed the schedule presented in the meeting agenda. (Attachment B). The meeting adjourned at 4:15 p.m.

Roll Call and Opening

Dr. Suhair Shallal, Designated Federal Officer for SGACS, called the roll of panel members, asked other persons participating via telephone to identify themselves, and welcomed participants to the teleconference.

Welcome

Dr. Henry Anderson, SGACS Chair, welcomed participants. He noted that the Panel consists of members from different backgrounds and committees, including the SAB Executive Committee (EC), SAB Environmental Health Committee (EHC), SAB Radiation Advisory Committee (RAC), the Children's Health Protection Advisory Committee (CHPAC), and the FIFRA Scientific Advisory Panel (SAP). In recognition of the different approaches and procedures of these various groups, Dr. Anderson encouraged members to raise any issues requiring clarification. Noting that the panel is working under a tight time line, he asked panel members to ensure that any concerns they might have are addressed.

Dr. Shallal thanked panel members for participating in the review and for their prompt responses to correspondence. She then provided a brief overview of the process by which the panel was formed. The newly-implemented SAB process for panel formation was modified to allow EPA to conduct an expedited review and to take advantage of the expertise of the FIFRA SAP and CHPAC. A document describing the process is available on-line and in hard copy. (Panel Formation Document, Attachment C) EPA adhered to the critical aspects of panel

selection, namely, perceived impartiality, knowledge and breadth of expertise, and panel balance, Dr. Shallal said. Any comments received during the public comment period, which ended March 18, 2003, were considered. The panel roster (Attachment A) and biosketches (Attachment D) are available on-line or in hard copy. Because this is not a "particular matter," the legal criteria for conflict of interest or impartiality were not met and waivers are not considered necessary for the panel members.

Dr. Vanessa Vu, SAB Staff Director, then thanked the panel members for their service and said that she was looking forward to a credible scientific review of this major Agency work product.

Ethics Briefing

Mr. Ken Wernick, Senior Ethics Counsel, highlighted aspects of the ethics statutes and regulations that were presented in detail in the ethics training module given on CD-ROM to panel members. Panel members are special federal employees during their time of service, and are subject to applicable statutes and regulations while performing their duties for the government.

For a "particular matter," federal officials are prohibited from participating if they themselves, or any members of their immediate families, have a financial interest in an entity that would be affected by the matter, Mr. Wernick noted. If a federal employee believes that the matter would affect members of his/her household, his/her employer, an organization in which he/she participates, etc., the federal employee should not act, but should call the matter to the attention of the DFO. Panel members must not accept any gifts that are based on their federal position, i.e., from any entity that may seek to do business with EPA. Exceptions to the rule include coffee and donuts, gifts of $20 or less, and gifts of personal friendship.

Mr. Wernick said that the ethics regulations also require panel members to not give preferential treatment to any entity or individual, that is, to always act impartially. Furthermore, panel members are prohibited from acting on "inside information"; such information is private to EPA and should not be released. Following their employment, panel members are prohibited from seeking employment from any entity that could benefit from the matter under consideration.

Public Comments

Mr. Lynn Ehrle, a senior research fellow for the Cancer Prevention Coalition, spoke about the discussion of radiation effects in the draft document. Mr. Ehrle proposed that the document does not adequately reflect the extensive literature on low-dose radiation exposure and cancer risk. Mr. Ehrle indicated that no one on the panel was from an independent public interest group. Mr. Ehrle urged the panel to look carefully at the literature on radiation. Dr. Shallal and Dr. Anderson invited Mr. Ehrle to submit his specific comments on the document in writing, including specific literature citations that he believes are missing.

Agency Briefing

Dr. Bill Wood, Risk Assessment Forum, thanked panel members for their willingness to participate. Dr. Wood noted that both the Guidelines and the SGACS document are currently out for public comment; the comment period was recently extended from May 1 until June 2. Any comments received by May 1 will be provided to the SGACS panel before its May 12-14 meeting, and a summary of comments received will also be presented at the meeting. Comments received after May 1 will also be provided to the panel.

Dr. Wood then reviewed EPA's reasons for deciding to issue two separate guidelines. One reason for having a separate SGACS document is that the Cancer Guidelines are in their third round of public comments, have undergone three prior SAB reviews, and have been the subject of substantial discussion in the scientific community, while the SGACS document is only now available for review for the first time. Second, in its 1999 recommendations, the SAB urged EPA to issue the Cancer Guidelines as promptly as possible and to address children's susceptibility in future revisions. Revising the entire Cancer Guidelines is a lengthy process, and the SAB noted that new science regarding susceptibility needs to be incorporated in a more rapid manner than would occur if entire new Cancer Guidelines were to be issued. Finally, consensus was not reached in the 1999 SAB review concerning additional safety factors for children; the SAB urged the Agency to continue considering this issue, and the current document reflects additional analysis and the SAB recommendation that position papers be prepared and tested. The SGACS document takes a weight of evidence approach, similar to the Cancer Guidelines, Dr. Wood said. It is mode of action based, which is also consistent with the Cancer Guidelines. EPA intends to update and add to the document on a regular basis. The SGACS document presents a default approach; consistent with the organization of the Cancer Guidelines. The assessor is instructed to start with data on a particular chemical and only turn to the default when data are lacking. EPA reviewed the available literature on tumor incidence for early-life vs. adult exposure and used it to estimate the difference in susceptibility over time. This proposed approach for assessing cancer risk has not been adopted by EPA yet, pending SAB review and public comment.

Dr. Melanie Marty asked for additional information on EPA's intent to revisit the SGACS document. Dr. Wood said that EPA would periodically look at the available science. The process generally takes two years from beginning to end, with peer review, etc., so the time frame would be unlikely to be shorter than that. Other documents on other modes of action could be underway concurrently, he noted.

Dr. Wood then reviewed the Charge Questions, which Dr. Shallal had sent to all members (Attachment E). The Agency is seeking a review of the soundness of the EPA position, namely, that its analysis and the underlying science support the conclusion that there is greater susceptibility to tumor development from early life exposure to mutagenic chemicals. Charge Questions 1 and 2 relate to the qualitative conclusions EPA has reached, dealing with the accuracy and objectivity of the underlying science and EPA's analysis and conclusions for chemicals acting through mutagenic and non-mutagenic modes of action. Charge Questions 3, 4, and 5 address quantitative aspects of the analysis, namely the approach to addressing the impact of early life exposures if there is differential life-stage susceptibility; the scientific

rationale for justifying the age groups of 0-2 and 2-15 years; and the sufficiency of the analysis and data supporting the adjustment factors. Charge Questions 6, 7, and 8 ask the panel for its recommendations on other modes of action that would be fruitful to assess in future guidelines; on how best to incorporate data from transplacental or *in utero* exposure; and on critical data needs to fill research gaps.

Dr. Anderson reviewed the allocation of responsibility for charge questions among the panel; each member is assigned to one question, but is asked to provide comments on all of the questions for discussion and integration into the final answers. Panel members should provide their comments to Dr. Shallal prior to the May 12 meeting; those individual comments will be made available to the public at the meeting. Panel members may share their comments with the other members assigned to their question, but need to send a copy of their comments to Dr. Shallal.

Discuss Structure of Face-to-Face Meeting

Dr. Anderson briefly reviewed plans for the May 12-14, 2003, meeting. The meeting will begin at 1:00 p.m. on May 12; this half-day session will be devoted to public comment and EPA presentations, although one EPA presentation will be given from 8:30-10:00 a.m. on May 13. Discussion of the charge questions will take place from 10:00 a.m. to 5:00 p.m. May 13. Forty five (45) minutes are allotted for discussion of each question. Breakout sessions will be held in the afternoon, allowing panel members to finalize their discussions and add to the draft text. Dr. Anderson asked that at least one person assigned to each question bring a computer to the meeting to facilitate editing. On May 13, Dr. Anderson and Dr. Shallal will begin working on the Executive Summary and letter to the Administrator.

On May 14, the draft text will be displayed on screen for further discussion, and the panel will ideally come to agreement in the morning, with the afternoon devoted to discussing key points in the Executive Summary and letter. The goal is to have a "first final" draft of the report by 5:00 p.m. on May 14.

Dr. Melanie Marty asked if the panel works by consensus, and how different views would be expressed. Dr. Anderson characterized consensus as the gold standard and the most useful to the Agency, but said that differing opinions will all be represented. Because the focus is the science, he said, panel members should support their alternative opinions with documentation and references.

Dr. Anderson asked if the panel would be interested in reading what other SAB reviews have said about the supplemental guidance. When members answered affirmatively, Dr. Wood noted that the July 1999 SAB review focusing on additions to the guidelines relating to children could be useful. Dr. Shallal will distribute this document to panel members.

Dr. Shallal reviewed travel arrangements for the meeting; a contractor is preparing itineraries, but panel members are responsible for making their own hotel reservations at the Sheraton Crystal City. No flights will be booked that depart before 6:30 p.m. on May 14.

Timetable:

For follow-up Conference Calls, Dr. Anderson said that he and Dr. Shallal intend to send out a final draft report on June 5, and to hold a conference call on or about June 11 to review the draft. Dr. Shallal will correspond with panel members via email to set a time for the conference call. Dr. Shallal and Dr. Anderson will circulate a "real final" document on June 25, allowing panel members a last time to comment. The report will go to the Executive Committee for approval at its July meeting.

The meeting was adjourned at 4:20 p.m.

Respectfully Submitted:

/Signed/

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Dr. Suhair Shallal
Designated Federal Official

Certified as True:

/Signed/

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Dr. Henry Anderson, Chair
Supplemental Guidance for Assessing Cancer Susceptibility (SGACS) Review Panel

ATTACHMENTS

Attachment A	Roster of SGACS Review Panel Members http://www.epa.gov/sab/pdf/sgacsrproster.pdf
Attachment B	Meeting Agenda http://www.epa.gov/sab/03agendas/sgacsrp042403a.pdf
Attachment C	Panel Formation Document
Attachment D	Panel Biosketches found at: http://www.epa.gov/sab/pdf/sgacsrpanel_bios_for_web.pdf
Attachment E	Charge Questions

ATTACHMENT E

QUESTIONS CONCERNING THE SUPPLEMENTAL GUIDANCE FOR ASSESSING CANCER SUSCEPTIBILITY FROM EARLY-LIFE EXPOSURE TO CARCINOGENS

The Agency seeks the Science Advisory Board's review of the soundness of the Agency's position that the Agency's analysis and the underlying scientific information support the conclusion that there is greater susceptibility for the development of tumors as a result of exposures in early lifestages as compared with adults to chemicals acting through a mutagenic mode of action.

1. Please comment on whether the Agency's analysis as applied to chemicals acting through a mutagenic mode of action is accurate, reliable, unbiased and reproducible. Likewise, please comment on whether the underlying scientific information used to develop the guidance is accurate, reliable, unbiased and reproducible. Are there any key studies that the Agency has overlooked in reaching this conclusion?

2. For chemicals acting through non-mutagenic modes of action, the Agency concludes that a range of approaches needs to be developed over time for addressing cancer risks from childhood exposures. Please comment on the Agency's conclusion that the scientific knowledge and data are insufficient at this time to develop generic guidance on how to address these chemicals and that a case-by-case approach is more suitable. Is the SAB aware of any additional data for chemicals acting through non-mutagenic modes of action relevant to possible early lifestage sensitivity?

3. Assuming that it is appropriate to conclude that there is differential lifestage susceptibility to chemicals acting through a mutagenic mode of action, the Agency's guidance uses a default approach that adjusts cancer slope factors (typically from conventional animal bioassays and/or epidemiologic studies of adult exposure) to address the impact of early lifestage exposure. Please comment on whether the approach is justified by the available data? Can the SAB suggest other approaches that might be equal or more appropriate?

4. When considering differential susceptibility, the Agency's guidance separates the potential susceptible period into two age groups, 0 - 2 years and 2 - 15 years. These groupings were based on biological considerations rather than exposure considerations. The first grouping, 0 - 2 years of age, is meant to encompass a period of rapid development and the second grouping, 2 – 15 years of age, was selected to extend through middle adolescence approximately following the period of rapid developmental changes during puberty. Please comment on the scientific rationale that was used to justify these age groupings. Can the SAB suggest other plausible ways to make these groupings?

5. The guidance provides a quantitative approach to account for the greater susceptibility of early-life exposure to chemicals that act through a mutagenic mode of action. An adjustment factor of 10 is applied to the cancer slope factor (derived from animal or epidemiology studies) for exposures before 2 years of age, a factor of 3 is applied for ages between 2 and 15 years, and no adjustment is applied after the age of 15. Please comment on whether the data and EPA

analysis are scientifically sufficient to support these adjustment factors. Are sufficient data, including breadth of chemicals, available to make these determinations?

OTHER QUESTIONS

6. The Agency recognizes that consideration of children's risk is a rapidly developing area and, therefore, the Agency intends to issue future guidance that will further refine the present draft guidance and possibly address other modes of action as data become available. The Agency welcomes the SAB's recommendations on other modes of action that may be most fruitful to assess in similar future analyses.

7. The analysis presented in the current Guidance relies on postnatal studies. Can the SAB recommend how to best incorporate data from transplacental or in utero exposure studies into future analyses?

8. The Agency welcomes the SAB's recommendations on critical data needs that will facilitate the development of future guidance addressing differential lifestage susceptibility.